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10/587,512	11/08/2007	Justin Hanes	JHUC-P01-021	3582

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EXAMINER	
SGAGIAS, MAGDALINE K	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,512	HANES ET AL.	
	Examiner	Art Unit	
	MAGDALENE SGAGIAS	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *3,4,6,9-11,14-16,19 and 23-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7,8,12,13,17,18,20-22 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments filed 08/26/2010 have been fully considered. Claims 1-29 are pending. The amendments to claims 1, 20 and the newly added claims 26-29 have been entered. Claims 3-4, 6, 9-11, 14-16, 19, 23-25 are withdrawn.

Claims 1-2, 5, 7-8, 12-13, 17-18, 20-22, 26-29 are under consideration.

For clarity of the record the examiner in the previous office action dated 05/26/2010, page 3, line 8 inadvertently included claims 9-10 as under consideration instead of including said claims in line 4 as withdrawn. Claims 9-10 are withdrawn in view of the Applicant's response to species election requirement dated 04/02/2010, page 2, last paragraph, wherein Applicants elected a therapeutic agent instead of an imaging agent for claim 7 and the generic claim 1 from which claim 7 is depended from. Therefore, currently the citation of claims 9-10 is corrected and claims 9-10 are currently correctly cited as withdrawn form consideration.

Second, Applicants argue that claim 19 should be included in Group I (i.e., as defined in the Restriction Requirement mailed July 21, 2009).1 As with the remaining claims of Group I currently under consideration, claim 19 is drawn to a polymeric particle comprising a pharmaceutically acceptable polymer core, a bioactive agent, and a surface-altering agent disposed on the surface of the core that renders the surface of the polymeric particle mucus resistant and/or enhances the average rate at which the particles or a fraction of the particles moves in mucus, wherein the bioactive agent is encapsulated in the polymer core. Accordingly, Applicants request claim 19 be considered with the remainder of the claims from Group I. These arguments are not persuasive because in response to the requirement for election of species, for the generic claims 1, 20 Applicant hereby elected bioactive agent; "a small molecule" for the bioactive agent a therapeutic agent which is a small molecule in response to election of species

requirement dated 04/02/2010 (see Response to Election / Restriction Filed 04/02/2010, page 2 last paragraph). Thus applicants elected a small molecule as a bioactive agent and not DNA as a bioactive agent for the generic claim 1 from which claim 19 is depended from. Therefore, claim 19 remains withdrawn from consideration.

Applicant's election of species "poly(D,L-lactic-co-glycolic) acid" for the polymer core; "a therapeutic agent" for the bioactive agent; "a small molecule" for the therapeutic agent; "polyethylene glycol" for the surface altering agent; and "chemoattractants" for the adjuvant dated 04/02/2010 for the generic claims 1, 20 is still acknowledged.

Claim Rejections - 35 USC § 102/Necessitated by Amendment

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The rejection of Claims **1-2, 7-8, 13, 17, 20, 21** under 35 U.S.C. 102(e) as being anticipated by **Alavattam et al** (US 7,060,299, filed 12/31/2003) is withdrawn in view of the newly added limitation to claims 1 and 20 dated 08/26/2010.

Applicant's arguments are directed to the newly added limitation to claims 1 and 20.

Claim Rejections - 35 USC § 103/Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims **1-2**, 5, 7-8, 11, 13, 17-18, 20-21, 26-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Alavattam et al** (US 7,060,299, filed 12/31/2003, (IDS)) in view of **Norris et al** (J Appl Poly Sci, 63: 1481-1492, 1997, (IDS)); **Quay et al** (US 7,157,426; continuation of application NO. 10/745,069, filed Dec. 23, 2003).

Alavattam et al discloses the encapsulation of spray dried chymotrypsin particles in the copolymers containing lactic acid and glycolic acid residues (poly(lactic acid-co-glycolic acid) or PLGA) coated with a cationic hydrophobic surfactant (CTAB) (column 13, example 6). Alavattam et al teaches that the microparticles containing gum arabic and the cationic surfactant (CTAB), not only control the release of the protein from PLGA microparticles, but also stabilize it prior to release over a period of at least about 3 weeks (Table 7) (**claims 1-2**, **5, 13, 20, 21** of the instant invention). Alavattam teaches therapeutic bioactive agents include small molecules such as monosaccharides disaccharides and detergents) (column 7, lines 60-66) (**claims 7-8** of the instant invention). Alavattam teaches the microparticles have a particle size range of about 1 to 150 um preferably particle size range of about 5 to 50 um (column 10, lines 6-11) **(claim 17).** Alavattam et al teach the generation of biodegradable and biocompatible microparticles that contain stabilized proteins and also control the kinetics of release of proteins over a period of several weeks under physiological conditions (column 1, lines 11-20). Alavattam et al teach stable protein microparticles encapsulated in hydrophobic poly(lactic-co-glycolic) acid polymers shows almost complete release of protein (about 80% of encapsulated protein is released after 28 days) and can release the protein in a near linear fashion over a period of about one month (column 1, lines 11-20). Alavattam et al suggest a "biologically

active protein" in the PLGA microparticles includes proteins and polypeptides that are administered to patients as the active drug substance for prevention of or treatment of a disease or condition as well as proteins and polypeptides that are used for diagnostic purposes, such as enzymes used in diagnostic tests or in vitro assays as well as proteins that are administered to a patient to prevent a disease such as a vaccine (column 6, lines 39-46). Alavattam et al teach stable protein microparticles encapsulated in hydrophobic biodegradable carriers such as poly(lactic-co-glycolic) acid polymers and surfactant surface altering agent referring to FIG. 4, this figure is a graph that shows the initial burst from microparticles containing stabilizer (gum arabic) and protein particles (CT) coated with different surfactants and encapsulated in PLGA: (1) and (2) stabilizer and 50 mM CTAB surfactant; (3) and (4) stabilizer and 50 mM DOTAP surfactant; (5) no stabilizer, 50 mM CTAB surfactant; (6) no stabilizer, 50 mM DOTAP surfactant; (7) no stabilizer, no surfactant; (8) stabilizer no surfactant. The axis are calibrated as follows, X=various formulations (1) through (8) above; Y=% cumulative release of protein in 24 hrs into phosphate buffered saline, pH 7.4. It is readily apparent that the positively charged surfactants in the presence of the negatively charged stabilizer decrease the initial burst substantially which meets the limitation comparing the polymeric particle with a surfactant to the same particle without the surfactant..

Alavattam et al do not specifically teach that the polymeric particle enhances the average rate at which the particles or a fraction of particles move in mucus by at least 5-fold compared to the same particles except without a surface-altering agent disposed on the surface.

However, at the time of the instant invention **Norris** teaches the surface charge and the hydrophobicity of the polystyrene microspheres (MS) play a role on the translocation of the microspheres through the gastrointestinal mucin (title, abstract) **(claim 18).** Norris teaches (MS)

have been proposed for use as oral vaccine delivery vehicles (VDV); the effects of size, z-potential, and surface hydrophobicity on the translocation (P_T) permeabilities of polystyrene (PS) MS with varying surface functional groups (amidine, carboxyl, carboxylate-modified [CML], and sulfate) were determined through gastrointestinal (GI) mucin (abstract). P_T were determined, under steady-state conditions, using a modified Ussing-type diffusion chamber and a mucin packet developed for use with the Transwell-Snapwell system (abstract). P_T followed the Stokes–Einstein relationship, demonstrating the limited ability of larger MS (.0.5 mm) to diffuse through the mucin layer. (abstract). P_T also varied according to the surface characteristics. Even though the z-potential did not correlate with the transport of MS through mucin, surface ionization appears to be important in MS translocation (abstract). The PS–amidine MS were significantly less hydrophobic and had a higher P_T than that of the other MS, suggesting that hydrophobicity is also a significant factor in MS transport through mucin (abstract). Norris teaches the appropriate formulas for enhancing the rate of particle transport by teaching the appropriate formulas, for determining the absolute surface hydrophobicity of the polymeric particle and (see p 1485, 1st column; p 1488, 2nd column; p 1489, 1st column).

Norris does not specifically teach a surface-altering agent on the surface of the MS enhances the average rate at which the particle move in mucus by at least 5-fold compared to the same particles except without a surface-altering agent disposed on the surface. However, at the time of the instant invention **Quay et al** (US 7,157,426; continuation of application NO. 10/745,069, filed Dec. 23, 2003) teach drug delivery systems based on biodegradable polymers for biomedical applications because such systems are non-toxic molecules [0198]. Quay teaches biodegradable polymers such as poly(D,L-lactic-co-glycolic acid) (PLGA), have received considerable attention for drug delivery carriers, since the degradation products of these polymers have been found to have low toxicity [0198]. Quay

teaches bioactive agents in a polymer core encapsulated in a surfactant [0165]. Quay teaches membrane penetration enhancing agents in the context of a surfactant, of the membrane penetration enhancing agents recited in (i)-(xix) [0166]. Certain surface-active agents are incorporated within the mucosal delivery formulations and methods of the invention as mucosal absorption enhancing agents [0167]. Quay teaches the mechanisms of action of these various classes of surface-active agents typically include solubilization of the biologically active agent. For proteins and peptides which often form aggregates, the surface active properties of these absorption promoters can allow interactions with proteins such that smaller units such as surfactant coated monomers may be more readily maintained in solution [0167]. Quay teaches examples of other surface-active agents which are more transportable units than aggregates [0167]. Quay teaches the surfactants to improve the transport characteristics of biologically active agents (including small molecule drugs) for enhanced delivery across hydrophobic mucosal membrane barriers, by surface charge modification of selected biologically active agents or delivery-enhancing agents described herein [0139] **(claim 8).** In this regard, the relative permeabilities of macromolecules is generally be related to their partition coefficients [0139]. The degree of ionization of molecules, which is dependent on the pK.sub.a of the molecule and the pH at the mucosal membrane surface, also affects permeability of the molecules [0139]. Quay teaches biologically active agents will be charge modified to yield an increase in the positive charge density of the biologically active agent [0141]. These modifications extend also to cationization of peptide and protein conjugates, carriers and other delivery forms disclosed herein [0141]. Cationization via a cationic surfactant offers a convenient means of altering the biodistribution and transport properties of proteins and macromolecules within the invention. Quay teaches agents in this context exhibit general or specific adhesion to one or more components or surfaces of the targeted mucosa [0232]. The

bioadhesive maintains a desired concentration gradient of the biologically active agent into or across the mucosa to ensure penetration of even large molecules (e.g., peptides and proteins) into or through the mucosal epithelium [0232]. Quay teaches employment of a bioadhesive within compositions of the invention yields a two- to five-fold, often a five- to ten-fold increase in permeability for peptides and proteins into or through the mucosal epithelium [0232] or at least 10-fold to 100-fold greater than permeability of Formulations A or B (peptide YY control) [0377]. This enhancement of epithelial permeation often permits effective transmucosal delivery of large macromolecules, for example to the basal portion of the nasal epithelium or into the adjacent extracellular compartments or a blood plasma or CNS tissue or fluid [0232]. Quay et al teach as an example, the bioavailability of 9-desglycinamide, 8-arginine vasopressin (DGAVP) intraduodenally administered to rats together with a 1% (w/v) saline dispersion of the mucoadhesive poly(acrylic acid) derivative polycarbophil, was 3-5-fold increased compared to an aqueous solution of the peptide drug without this polymer [239] **(claims 26-27).** Quay teaches in addition to protecting against enzymatic degradation, bioadhesives and other polymeric or non-polymeric absorption-promoting agents for use within the invention may directly increase mucosal permeability to biologically active agents to facilitate the transport of large and hydrophilic molecules, such as peptides and proteins, across the nasal epithelial barrier, mucoadhesive polymers and other agents have been postulated to yield enhanced permeation effects beyond what is accounted for by prolonged premucosal residence time of the delivery system [0241].

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007): "Exemplary

rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Accordingly, it would have been obvious to the ordinarily skilled artisan to modify the teachings of Alavattam to utilizing the formulas, such as that taught by Norris, to determine the effect of size, surface charge and hydrophobicity, in order to determine the rate of particle transport as taught by Norris, and to detect the hydrophobicity of the polymeric particles, with a reasonable expectation of success. One of ordinary skill in art would have been motivated to make a polymeric particle utilizing poly(D,L-lactic acid-co-glycolic acid) for encapsulating biodegradable biological agents utilizing as surfactant altering agent in view of the teachings of Quay cationization via a cationic surfactant offers a convenient means of altering the biodistribution and transport properties of proteins and macromolecules across mucosal surface (mucus) and cationization increases the transport of biomolecules across mucosal surface. This is further underscored by the teachings of Alavattan who teach that PLGA microspheres can include therapeutic bioactive agents such as small molecules such as monosaccharides

disaccharides and detergents) (column 7, lines 60-66) and as well as proteins that are administered to a patient to prevent a disease such as a vaccine (column 6, lines 39-46) and the teachings of Quay that Surface hydrophobicity is an important factor in the transport of particles across mucus.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of

Applicant's arguments are moot because they are directed to the newly added limitation to claims 1 and 20.

Claims 1, **12** is rejected under 35 U.S.C. 103(a) as being unpatentable over Alavattam et al (US 7,060,299, filed 12/31/2003 (IDS)) in view of Norris et al (J Appl Poly Sci, 63: 1481-1492, 1997 (IDS)); Quay et al (US 7,157,426; continuation of application NO. 10/745,069, filed Dec. 23, 2003) and further in view of **Singh et al,** (PNAS, 97(2): 811-816, 2000, (IDS).

The teachings of Alavattan/Norris/Quay apply here as set forth above.

Alavattan/Norris/Quay does not specifically teach the polymetic particle further comprising an adjuvant.

However, at the time of the instant invention **Singh et al** teaches biodegradable microparticles with a cationic surface was developed to improve the delivery of adsorbed DNA into antigen-presenting cells after intramuscular injection (abstract). Singh teaches after i.m. immunization, the microparticles induced significantly enhanced serum antibody responses in comparison to naked DNA, the level of antibodies induced by the microparticles was significantly enhanced by the addition of a vaccine adjuvant, aluminum phosphate (abstract). Singh teaches by the addition of aluminum phosphate to the PLG/CTAB microparticles, resulted in a significantly enhanced response over that achieved with microparticles alone (p 815, 2nd column, 1st paragraph). An important advantage of the microparticle DNA delivery is flexibility,

allowing additional components, e.g., adjuvant, to be entrapped in the particles carrying DNA, entrapped into separate particles and mixed with DNA particles, adsorbed to the surface of additional particles, or any combination of the above (p 815, 2nd column, 1st paragraph).

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention."

Accordingly, it would have been obvious to the ordinarily skilled artisan to modify the teachings of Alavattan/Norris/Quay to include an adjuvant in the polymeric particle, such as that taught by Singh, with a reasonable expectation of success. One of ordinary skill in art would have been motivated to include an adjuvant in the polymeric particle of Alavattan/Norris/Quay because Singh teaches by the addition of aluminum phosphate to the PLG/CTAB

microparticles, resulted in a significantly enhanced response over that achieved with microparticles alone (p 815, 2nd column, 1st paragraph). An important advantage of the microparticle DNA delivery is flexibility, allowing additional components, e.g., adjuvants, to be entrapped in the particles carrying DNA, entrapped into separate particles and mixed with DNA particles, adsorbed to the surface of additional particles, or any combination of the above (p 815, 2nd column, 1st paragraph).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Applicant's arguments are moot because they are directed to the newly added limitation to claims 1 and 20.

Claims 1, **22** is rejected under 35 U.S.C. 103(a) as being unpatentable over Alavattam et al (US 7,060,299, filed 12/31/2003, (IDS)) in view of Norris et al (J Appl Poly Sci, 63: 1481-1492, 1997, (IDS)); Quay et al (US 7,157,426; continuation of application NO. 10/745,069, filed Dec. 23, 2003) and further in view of **Baichwal et al** (U.S. Patent No. 5,612,053 (IDS)).

The teachings of Alavattam/Norris/Quay/ apply here as set forth above.

Alavattam/Norris/Quay does not specifically teach an inhaler.

However at the time of the instant invention Baichwal teaches controlled release powder insufflation formulations containing medicament and a controlled release carrier. Baichwal teaches that the compositions may be prepared by blending fine drug particles (0.1-10 microns) with fine polysaccharide particles (0.1-10 microns) (col. 9, lines 27-31). Baichwal teaches that a wide variety of medicaments can be utilized in the dry powder inhalation/insufflation formulations of the present invention, including anticholinergic agents, corticosteroids, posterior pituitary hormones, cytokines, cytokine inhibitors, polypeptides, peptides, enzymes, genes,

gene fragments, hormones (col. 10, lines 1-65). Baichwal teaches that the formulations of his invention may be adapted for use with respect to any oral and/or nasal insufflation device for powdered or solid medicaments (col. 11, lines 17-19).

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Alavattam/Norris/Quay and Baichwal, because both inventors teach dry powder pharmaceutical compositions for delivery to the lungs. Inhalation is the delivery of a medicated to the lungs or other body cavity. It would have been obvious to a skilled artisan that oral/nasal inhalation would deliver a medicated PLGA microsphere to the lungs. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings, because both references teach dry powder pharmaceutical compositions wherein the microsphere particles are small (10 microns or less) and are intended for delivery to the lungs.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Applicant's arguments are moot because they are directed to the newly added limitation to claims 1 and 20.

Claims 1, **28-29** is rejected under 35 U.S.C. 103(a) as being unpatentable over Alavattam et al (US 7,060,299, filed 12/31/2003, (IDS)) in view of Norris et al (J Appl Poly Sci, 63: 1481-1492, 1997, (IDS)); Quay et al (US 7,157,426; continuation of application NO. 10/745,069, filed Dec. 23, 2003) and further in view of **Dawson et al** (Vet Rec, 127(13):338, 1990).

The teachings of Alavattam/Norris/Quay/ apply here as set forth above.

Alavattam/Norris/Quay does not specifically teach a pig gastric mucus.

However, at the time of the instant invention Dawson teaches primary parenteral transmission of bovine spongioform encephalopathy to the pig (title).

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Alavattam/Norris/Quay andDawson, because both inventors teach pharmaceutical compositions for delivery via mucosal barrier. Primary parenteral transmission of bovine spongioform encephalopathy to the pig it would have been obvious to a skilled artisan that parenteral administration of bovine spongioform encephalopathy to the pig would deliver a medicated PLGA microsphere to the brain. A skilled artisan would have had a reasonable expectation of success upon combination of the prior art teachings, because both references teach pharmaceutical compositions wherein the microsphere particles are intended for delivery to the brain via transport thru the GI mucus as an experimental animal model.

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571)272-3305. The examiner can normally be reached on Monday through Friday from 9 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paras Peter can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Magdalene K. Sgagias,
Patent Examiner, Art Unit 1632

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632